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A Randomized Study of Imipenem Compared to Cefotaxime plus Piperacillin as Initial Therapy of Infections in Granulocytopenic Patients

Summary: The objective of the presented, randomized study was to compare the efficacy of antimicrobial monotherapy with imipenem ($3 \times 0.5 \text{ g/d}$) to a combination therapy with cefotaxime ($3 \times 2 \text{ g/d}$) plus piperacillin ($3 \times 4 \text{ g/d}$) for empirical treatment of infections in neutropenic patients. In 165 patients, 237 infectious episodes were evaluable. The overall response rate of patients treated with cefotaxime plus piperacillin was 67/115 (58%), of those treated with imipenem 66/122 (54%). In patients not responding to the initial therapy regimen within 2 or 3 days, the antimicrobial therapy was modified. After therapy modification 85/100 patients were cured. Fever of unknown origin (FUO) showed the most favourable course compared to other infection types, with a response in 46/59 (78%) and in 35/50 (70%) cases, respectively. In comparison, pneumonias were successfully treated in only 3/21 (14%) and 7/37 (19%) cases. Even including patients with modified therapy, only 66% (21/32) of pneumonia episodes responded. The unfavourable results in pneumonias is mainly due to the high rate of 13 systemic mycoses in this group (22%). Overall, a similar response was observed in patients treated with cefotaxime plus piperacillin in comparison with imipenem. In primary bacteremias however, an advantage was observed in patients treated with imipenem (20/27; 74%) compared with cefotaxime plus piperacillin (11/23; 48%).

Introduction

Severe, life-threatening infections are a major risk for patients with hematologic malignancies undergoing intensive chemotherapy with its long-term granulocytopenia [1,2]. Up to now empiric broad-spectrum antibiotic combination therapy is the accepted practice of treatment in febrile granulocytopenic patients. Combinations usually include an aminoglycoside plus an extended-spectrum cephalosporin or penicillin or two β -lactam antibiotics. In the last decade, gram-positive bacteria and especially fungi have emerged as increasingly frequent pathogens resulting in empirical several-step treatment regimens [1,3–7]. But also cost-effective, less toxic monotherapies, e.g. with imipenem or ceftazidime, have been investigated in febrile neutropenic patients, compared to combination therapy or to one another. The study results (Table 1) have indicated that combination and monotherapy are similarly effective [8–17]. Monotherapy, however, has been controversially discussed especially because of resistance problems. Ceftazidime is more effective than imipenem in the treatment of *Pseudomonas* sp., but less active against gram-positive cocci in comparison to other cephalosporins; about 20% of *Pseudomonas aeruginosa* and more than 80% of *Stenotrophomonas maltophilia* strains are resistant against imipenem, whereas imipenem is the most effective β -lactam against gram-positive cocci (except oxacillin-resistant staphylococci) compared with other β -lactams [18,19]. Furthermore, imipenem has an acceptable spectrum of side-effects and no essential organospecific toxicity. Mostly, imipenem has been used at a dose of $4 \times 0.5 \text{ g}$ to $4 \times 1.0 \text{ g}$ (Table 1) per day with success rates ranging from 70% to 90%. A non-comparative, open pilot

study performed by our group with imipenem at a dose of 1.5g per day resulted in a satisfactory response of 65% [20]. Thus a larger open prospective, randomized study was planned to compare the efficacy of monotherapy with imipenem to a "standard" combination therapy (cefotaxime plus piperacillin) as initial treatment of infections in granulocytopenic patients. Interim results of this study have been reported at the Annual Congress of the German and Austrian Society of Hematology and Oncology in Essen, October 10–13, 1993 [21].

Patients and Methods

Study design: This was an open, prospective randomized study in which patients were enrolled after informed consent was obtained. Patients were centrally randomized by the physician on duty in the emergency room not participating in the study.

Patient selection: Patients with the following diagnoses were entered into the study: acute leukemia, chronic myelogenous leukemia with blast excess, Hodgkin's disease, myelodysplastic syndrome RAEB and RAEB-T, non-Hodgkin's lymphoma. Inclusion criteria were fever of $\geq 38.0^\circ\text{C}$ and granulocytopenia $< 1,000/\mu\text{l}$. Patients with suspected non-infectious fever (for example transfusion reaction, drug fever), age < 18 and > 80 years, known hypersensitivity against β -lactams, intravenous antibiotic therapy < 7 days prior to randomization were excluded. Patients

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Table 1: Response rates of antimicrobial mono and combination therapy in infections of granulocytopenic patients.

Authors	Therapy	Response (%)
Pizzo et al. 1986 [15]	Ceftazidime	89
Norrby et al. 1987 [13]	Imipenem (4.0 g/day)	81
Walther et al. 1989 [22]	Imipenem (1.5 g/day)	65
Liang et al. 1990 [11]	Ceftazidime Imipenem (2.0 g/day)	56 77
Winston et al. 1991 [17]	Double β -lactam Imipenem (2.0-4.0 g/day)	75 82
Cornelissen et al. 1992 [9]	β -lactam/aminoglycoside Imipenem (2.0 g/day)	74 91
PEG* study, 1994 [6]	Double β -lactam β -lactam/aminoglycoside	65 70

*PEG: Paul Ehrlich Society.

Table 2: Patient characteristics.

	CEF/PIP		IMI	
	N	%	N	%
Episodes	115	100	122	100
Age: mean/range (years)	47(17-75)		44(17-72)	
Diagnoses:	AML	65 57	66	54
	ALL	14 12	16	13
	NHL	30 26	33	27
	others	6 5	7	6
Remission induction	40	35	34	28
Remission	48	42	52	43
Progression	12	10	12	10
Relapse	15	13	24	19
Neutropenia from start of fever (days)				
	1-12	68 59	62	51
	> 12	23 20	24	19
	Not evaluable	24 21	36	30

N: number; CEF/PIP: cefotaxime/piperacillin; IMI: imipenem.

were allowed to reenter the study for a second infectious episode provided the episodes were more than 4 weeks apart.

Procedures: Before the start of antibiotic therapy all patients underwent a thorough physical examination and chest x-ray. Specimens for cultures, at least two blood cultures from peripheral veins and central venous catheters, cultures from urine, throat and other suspected sites were collected. In patients with no response to the initial therapy the procedures were repeated before

modification of antibiotic therapy. In patients with pneumonia and in those not responding after 6 days of antibiotic treatment, a thoracic CT-scan was taken for establishing a pulmonary aspergillosis even at an early stage of disease [22]. If possible, a bronchoalveolar lavage was obtained in patients with pneumonia. Moreover, the following serologic tests were performed: herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein Barr virus, *Aspergillus*, *Candida*, and in pneumonia patients, additionally *Chlamydia*, *Mycoplasma* and *Legionella*.

Treatment: The patients were randomized to receive daily either cefotaxime 3x2g plus piperacillin 3x4g or imipenem/cilastatin 3x0.5g as a short infusion [20]. Patients who did not respond after 48-72 h to initial therapy were additionally treated with gentamicin 3x 40 mg daily. In patients with microbiologically proven documented infection, the antibiotic therapy was modified according to susceptibility testing. In responders with persistent granulocytopenia the regimen was continued for at least 5 days, with increasing granulocytes for 3 days after defervescence. In patients with pneumonia the antibiotic treatment was given until complete regression of the pulmonary infiltrates.

Classification of infection: The following types of infection were defined: 1) FUO (fever of unknown origin) – suspected infection without pathogen identification or infectious foci, 2) pneumonia without detectable pathogen, 3) pneumonia with evidence of an infectious agent proven by microbiological, serological or radiological methods or by autopsy, 4) primary bacteremia: positive blood culture or catheter luminal cultures without infectious focus, 5) others – clinically documented infections, except pneumonias, with or without proven pathogens.

Evaluation of response: Response was defined as stable defervescence and complete regression of infectious foci without any modification of initial antibiotic therapy. A non-response was defined as initial transient defervescence with recurrence of fever, or clinical progression and lack of defervescence within the first 3 days, which resulted in therapy modification. In some patients the initial therapy without modification was continued in spite of persistent fever > 38.0°C. These patients showed improvement of other clinical features or had a causative organism identified which proved to be susceptible to initial treatment. These episodes were defined as delayed response. The infectious episodes were followed until remission or death of patients even if the study was finished earlier.

Statistics: Statistical significance was calculated by Fisher's exact test.

Results

Patient Characteristics

From July 1990 to July 1993, 195 neutropenic patients with 267 infectious episodes entered the study; 237 episodes were evaluable. In 115 episodes cefotaxime plus piperacillin were administered, 122 were treated with imipenem/cilastatin. There were no differences between the randomization arms in age, sex, diagnosis, remission status of malignancy, duration of granulocytopenia (Table 2), central venous catheters (29% vs. 36%), corticosteroids (31% vs. 28%) or therapy with hematopoietic growth factors G-CSF or GM-CSF (37% vs. 43%). In 50% vs. 48% of the episodes, the patients received antibacterial prophylaxis with co-trimoxazole, in 23% vs. 28% with ciprofloxacin.

The classification of infection is listed in Table 3. The majority of the patients was diagnosed as FUO. In 16 episodes (7%) an abdominal, in six (3%) a skin infection was diagnosed. Three patients suffered from infection of ENT and two from urinary tract infections.

Microorganisms

Forty-one/one hundred fifteen and 51/122 episodes in the combination and imipenem group, respectively, were microbiologically documented (Table 4). In both groups gram-positive organisms (only episodes with at least two positive cultures from peripheral vein or central venous catheter were accepted) were isolated more frequently than gram-negative bacteria. Thirteen patients were diagnosed to have systemic fungal infection, in most cases *Aspergillus fumigatus* was found. Viral infections and infections caused by *Chlamydia*, *Mycoplasma*, mycobacteria and anaerobes were rare. The pathogens were isolated from peripheral veins in 90% (in 21% of them additionally from central venous catheters).

Out of 58 pneumonias only 34 were microbiologically documented. 19 gram-positive, ten gram-negative, 13 fungi and four other microorganisms (mycobacteria, anaerobes, *Mycoplasma* and adenovirus) were diagnosed. Twelve patients had mixed infections.

Sixty-four percent of the pathogens were diagnosed on the first day of fever: 85% of those found in primary bacteremias, 36% of organisms causing pneumonias and 75% of those in other infections. In 45% of the pneumonia episodes the pathogen was diagnosed after the fifth febrile day. Most of these pathogens were fungi, but also gram-positive bacteria.

Clinical Outcome

Fifty-eight percent of the episodes treated with cefotaxime plus piperacillin and 54% treated with imipenem responded (n.s., Table 5). The cure rate of the FUO episodes was 78% vs. 70%, of pneumonias 14% vs. 19%, respectively (only clinically documented 33% vs. 40%, with proven pathogens 0% vs. 5%). The patients with primary bacteremias responded in 48% vs. 74% ($p=0.08$) and other infections in 58% vs. 50% of the episodes. Though not statistically significant, more patients with positive blood cultures responded to empirical treatment with imipenem (75%) than the combination arm (48%). Table 6 shows the better response of the pathogens in primary bacteremias than in pneumonias and other clinically documented infections. One hundred episodes without response of initial therapy regimens were additionally treated with gentamicin or according to susceptibility, resulting in an 85% response rate.

Twenty-three (10%) patients died during the infectious episode. In 14 cases an autopsy was performed. The causes of death were defined according to autopsy results or clinical course: Infection as cause of death was seen in 70%, the other patients died from their malignancy and/or

Table 3: Classification of infection.

	CEF/PIP		n.s.	IMI	
	N	%		N	%
FUO	59	52	n.s.	50	41
Pneumonia	21	18	n.s.	37	30
Only clinically documented	9	8	n.s.	15	12
With documented pathogen	12	10	n.s.	22	18
Primary bacteremia	23	20	n.s.	27	22
Others	12	10	n.s.	8	7
Total	115	100	n.s.	122	100

N: number; CEF/PIP: cefotaxime/piperacillin; IMI: imipenem.

Table 4: Isolated organisms.

	CEF/PIP		N	% of episodes	IMI	
	N	%			N	% of episodes
All episodes	115		122			
All pathogens	48*		62**			
Episodes with documented pathogen	41		51			
Gram-positive	24	21	30	25		
<i>Staphylococcus epidermidis</i>	10	9	11	9		
Viridans streptococci	9	8	7	6		
<i>Streptococcus mitis</i>	5		3			
<i>Staphylococcus aureus</i>	3		3			
Others	2		9	7		
Gram-negative	15	13	20	16		
<i>Escherichia coli</i>	9	8	12	10		
<i>Pseudomonas aeruginosa</i>			3			
<i>Pseudomonas non aeruginosa</i>	2		1			
<i>Klebsiella</i> spp.			1			
Others	4	3	3			
Anaerobes	1		1			
<i>Mycobacterium tuberculosis</i>			1			
Fungi	5	4	8	7		
<i>Aspergillus</i> ssp.	4	3	6	5		
<i>Candida albicans</i>			2			
<i>Candida tropicalis</i>	1					
Virus	3		2			

N: number; *: seven mixed infections; **: 11 mixed infections.

Table 5: Response to therapy.

	CEF/PIP		n.s.	IMI		
	R/N	%		R/N	%	
FUO	46/59	78		35/50	70	
Pneumonia	3/21	14	n.s.	7/37	19	
Only clinically documented	3/9	33	n.s.	6/15	40	
With documented pathogen	0/12	0	n.s.	1/22	5	
Primary bacteremia	11/23	48	p=0.08	20/27	74	
Others	7/12	58	n.s.	4/8	50	
Total	67/115	58	n.s.	66/122	54	
Defervescence (day)	1-3	52/67	78	n.s.	50/66	76
	4-7	15/67	22	n.s.	15/66	24
	>7	0/67	0	n.s.	0/66	0

R: responders; N: number of episodes.

bleeding complications. No infection-related death occurred in patients with FUO, but 35% of the deaths in patients with pneumonias and a proven pathogen were caused by infection. Three of the latter patients had a refractory malignancy. In 7/23 patients *A. fumigatus* was proven. Two patients died from ARDS in viridans streptococcal bacteremia, two each from *Staphylococcus aureus* sepsis and fatal necrotizing colitis.

Table 6: Response rates (R) of various microorganisms in primary bacteremias in comparison to clinically and microbiologically documented infections.

	CEF/PIP				IMI			
	Primary bacteremia		Clinical microbiological		Primary bacteremia		Clinical microbiological	
	N	R (%)	N	R (%)	N	R (%)	N	R (%)
Gram-positive	18	44	6	0	15	71	15	14
<i>Staphylococcus epidermidis</i>	8	63	2	0	5	80	6	33
Viridans streptococci	6	17	3	0	4	50	3	0
<i>Streptococcus mitis</i>	3	33	2	0	2	50	1	0
<i>Staphylococcus aureus</i>	3	33					3	0
Gram-negative	6	50	9	11	14	79	6	0
<i>Escherichia coli</i>	5	60	4	0	10	80	2	0
<i>Pseudomonas aeruginosa</i>	0		0		2	100	1	0
<i>Pseudomonas non-aeruginosa</i>	0		2	0			1	0
<i>Klebsiella</i> spp.	0		0		1	100	0	

Prognostic Factors

The increase of granulocytes was the most important prognostic factor resulting in response rates of 96% and 98% (cefotaxime/piperacillin and imipenem, respectively) compared to 28% and 33% with persistent granulocytopenia (Table 7). Prolonged granulocytopenia from start of fever was correlated with decreasing response: 88% and 87% with neutropenia of 1-3 days, 37% and 34% with neutropenia > 7 days. The different responses of AML, ALL and NHL are caused by the different duration of granulocytopenia due to various chemotherapy regimens. Central venous catheters had no influence on response rates (removal of catheters was not necessary as all patients with positive catheter cultures improved soon after start of antibiotic therapy). Primary pneumonias or other clinically documented infections diagnosed within the first 3 days of fever had an overall response rate of 50% compared to 7% when diagnosed later.

Adverse Events

Hypersensitivity occurred in four (3%) of the patients treated with cefotaxime plus piperacillin, in three (2%) of the patients treated with imipenem. Seven (6%) of the patients in the imipenem group suffered from nausea (WHO grade 1-2), in two patients nausea improved when infusion time was increased, in one patient by prophylaxis with alizapride. Nephro- or hepatotoxicity did not occur; there were no signs of CNS-symptoms under imipenem.

Discussion

The initial monotherapy with imipenem resulted in similar efficacy compared to the combination of cefotaxime

with piperacillin (response rate 58% vs. 54%, n.s.). Both therapy groups were identical with respect to time until defervescence. Similar response rates of monotherapy compared to combinations have been reported in previous trials. In the first trials carried out in the early eighties predominantly ceftazidime was investigated. The response rates with ceftazidime were 89% compared to 78% of cephalothin/gentamicin/carbenicillin [15] and 79% vs. 61% with ceftazidime/piperacillin [3]. In recent years, imipenem has been investigated as monotherapy. Imipenem treatment resulted in cure rates of 81% in comparison to 63% with amikacin/piperacillin [13], 81% compared to 78% of cefotaxime/piperacillin and 82% with ceftazidime/piperacillin [17]. Imipenem was as effective as cefuroxime/gentamicin or cephalothin/gentamicin (91% vs. 74%) [9]. In comparison with ceftazidime, there was no significantly different cure rate (56% vs. 77%) [11]. Prospective, randomized trials have not reported any essential difference of efficacy in monotherapy with imipenem or ceftazidime compared to the combination treatments. The lower total response rates in our study may be due to the inclusion of patients with predominantly acute leukemias who have longer periods of granulocytopenia than patients with solid tumors.

Although study results have not reported significant dif-

ferences of efficacy between combination and monotherapy, combination therapy has been widely recommended, especially in documented infections [15]. Recent studies using imipenem, however, suggest at least similar response rates compared to combination therapy even in documented infections. In primary bacteremias, therapy with imipenem appears to be more advantageous than the combination therapy applied (89% vs. 53%), as reported by *Cornelissen* [9] and by our own study (74% vs. 48%). Whether the high response rate to imipenem is due to lower endotoxin release, as reported by *Dofferhoff* and colleagues, can be debated [23]. Likewise, a more favourable outcome of only clinically documented infections with imipenem compared to combination has been found (88% vs. 58–60%) [17].

In various infection types, we noted essential differences of cure rates: FUO 74%, bacteremias 62%, pneumonias 17%, which responded most unfavourably. Similar findings have been reported in the study of the Paul Ehrlich Society (PEG) with response of 65–71% in FUO episodes and about 60% in pneumonias [6]. Other authors also reported an unfavourable outcome in pneumonias compared to FUO with 41%–63% vs. 77%–81% [10] or 43%–60% vs. 67%–74% [11]. In our study, pneumonias with documented pathogens had especially low response

Table 7: Response in correlation with various factors.

			CEF/PIP			IMI		
			N	R (%)		N	R (%)	
Increasing granulocytes	yes		49	47 (96)	n.s.	40	39 (98)	
	no		64	18 (28)	n.s.	82	27 (33)	
Neutropenia from start of fever (days)		1–3	16	14 (88)	n.s.	15	13 (87)	
		4–7	35	26 (74)	n.s.	33	25 (76)	
		8–11	17	8 (47)	n.s.	14	6 (43)	
		>12	23	7 (30)	n.s.	24	7 (29)	
Central venous catheter	yes		29	16 (55)	n.s.	36	16 (44)	
	no		86	51 (59)	n.s.	86	50 (58)	
Malignancy	AML		65	31 (48)	n.s.	66	27 (41)	
	ALL/AUL		14	9 (64)	n.s.	16	11 (69)	
	NHL		30	25 (83)	n.s.	33	24 (73)	
Remission status	remission		48	33 (69)	n.s.	52	37 (71)	
	remission induction		40	22 (55)	n.s.	34	15 (44)	
	progression		12	6 (50)	n.s.	12	4 (33)	
	relapse		15	6 (40)	n.s.	24	10 (42)	
Documentation of focus	day	1–3	15	9 (60)	n.s.	25	11 (44)	
		4–7	11	1 (9)	n.s.	14	1 (7)	
		>7	7	0	n.s.	11	1 (9)	
Documentation of pathogen	day	1–3	37	13 (35)	n.s.	44	24 (55)	
		4–7	7	0	n.s.	3	1 (33)	
		>7	4	0	n.s.	15	0	

rates, caused by the high incidence of fungi, partially *Aspergillus*, which was seen in 10/58 pneumonia episodes. The results of the PEG study have drawn attention to the problem of pulmonary mycoses [6] reporting a high incidence of fungi especially in pneumonias occurring in the late infection stage. Thus an early empirical treatment with antimycotics in pneumonia episodes is recommended and is under investigation in ongoing trials using amphotericin B (present study of PEG [24]) or fluconazole [25]. But not only fungal pneumonias caused worse response in pneumonia patients: 5/10 gram-negative, all streptococcal infections, 2/3 *S. aureus* and 4/5 *Staphylococcus epidermidis* infections with pulmonary infiltrates failed to respond in the first 72 h and were rated as failures. None of the strains was resistant *in vitro* to the study drugs and thus the susceptibility pattern cannot explain the poor response rate in pneumonia.

The microorganisms, mostly found in our study patients, were gram-positive bacteria (23%) followed by gram-negatives and fungi (15% and 5%, respectively). The most frequent fungus was *Aspergillus* (ten episodes), systemic *Candida* infections were rarely seen (three episodes). These results disagree with those of other studies observing *Candida* sp. to be the predominant fungi [1, 6].

Resistance against imipenem especially in *Pseudomonas* sp. and coagulase-negative staphylococci is one of the main objections to initial monotherapy with imipenem. An analysis of resistance patterns at the Centre of Internal Medicine, University Frankfurt, between 1990 and 1992 has not shown an increase of imipenem-resistant *P. aeruginosa* strains (17% to 16%). Moreover, *P. aeruginosa* bacteremias were rarely seen in our study patients. Over the year there has been an increase from 17% to 23% in imipenem-resistant coagulase-negative staphylococci. However, as these bacteremias are not fulminant, treatment modification was initiated after the results of sensitivity testing became available. None of the patients with a bacteremia with *S. epidermidis* died. In contrast to favourable courses of most infections due to gram-positive bacteria, infections caused by streptococci of the viridans

group, particularly *Streptococcus mitis*, have been reported to be associated with a high rate of lethal courses by development of ARDS [26]. The empirical treatment with vancomycin-containing combinations has been widely discussed. The PEG study has not observed any advantage of additional treatment with vancomycin in non-responders of initial therapy [6]. In contrast, several randomized studies reported more favourable results in patients with initial treatment with vancomycin [7,27].

The duration of granulocytopenia was found to be the main prognostic factor for the outcome of infections, as also described by others [3,6,10]. The importance of the duration of granulocytopenia on occurrence and course of infection is reflected by the recommendation of colony-stimulating factors (G-CSF or GM-CSF) [14]. Using G-CSF a shortening of granulocytopenic period and activation of granulocyte function can be achieved [28–30]. In patients with acute lymphoblastic leukemia simultaneously receiving chemo-radiotherapy and randomized G-CSF vs. placebo severe infections such as sepsis or pneumonia occurred in 14% of the G-CSF group, but in 30% of the placebo group [29].

In conclusion, the initial monotherapy with imipenem can be recommended in infections of granulocytopenic patients. Monotherapy with a drug such as imipenem can be more cost-effective in initial empirical treatment in such patients. Increasing incidence of systemic mycoses, especially in patients with pulmonary lesions, would warrant an early empiric antimycotic treatment. Colony-stimulating factors for earlier hematopoietic reconstitution and activation of neutrophil function should be considered in febrile patients with long-term granulocytopenia.

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Zusammenfassung: Randomisierte Studie mit Imipenem versus Cefotaxim/Piperacillin in der Initialtherapie von Infektionen granulozytopenischer Patienten. Ziel der vorliegenden prospektiven, randomisierten Studie¹ war der Vergleich der Effektivität einer Monotherapie mit Imipenem (3×0,5g/Tag) gegenüber einer Kombinationstherapie mit Cefotaxim (3×2g/Tag) plus Piperacillin (3×4g/Tag) in der Initialtherapie von Infektionen granulozytopenischer Patienten. 237 Infektionsepisoden bei 165 Patienten waren evaluierbar. Insgesamt wurde unter Cefotaxim plus Piperacillin eine Heilung in 67/115 (58%), unter Imipenem in 66/122 Episoden (54%) erzielt. Bei Nichtansprechen innerhalb von drei Tagen unter der Initialtherapie wurde die antibiotische Behandlung modifiziert. Hierdurch wurde bei weiteren 85/100 Patienten eine Heilung

erreicht. Unter den verschiedenen Infektionstypen war die Ansprechrate bei Fieber unklarer Genese (FUO) am höchsten mit einem Therapieerfolg in 46/59 Episoden unter Cefotaxim plus Piperacillin (78%) sowie in 35/50 Fällen unter Imipenem (70%). Besonders ungünstig verliefen dagegen die Pneumonien mit einem Ansprechen in 3/21 (14%) bzw. in 7/37 (19%) der Fälle. Auch unter Therapiemodifikation ergab sich hier eine Ansprechrate von insgesamt lediglich 66% (21/32). Die ungünstigsten Ergebnisse bei diesem Infektionstyp sind hauptsächlich durch den hohen Anteil von 13 systemischen Pilzinfektionen bei den Pneumonien (22%) bedingt. Insgesamt zeigten sich keine signifikanten Unterschiede in der Ansprechrate unter Cefotaxim plus Piperacillin im Vergleich zu Imipenem. Bei den primären Bakteriämien zeigte sich jedoch eine höhere Ausheilungsrate unter Imipenem mit 20/27 Episoden (74%) im Vergleich zu Cefotaxim plus Piperacillin mit 11/23 (48%) Episoden.

¹Zwischenergebnisse dieser Studie wurden auf der Gemeinsamen Jahrestagung der Deutschen und Österreichischen Gesellschaft für Hämatologie und Onkologie in Essen, 10.–13.10.93 vorgetragen.

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